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Understanding, justifying, and optimizing radiation exposure for CT imaging in nephrourology

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Abstract

An estimated 4–5 million CT scans are performed in the USA every year to investigate nephrourological diseases such as urinary stones and renal masses. Despite the clinical benefits of CT imaging, concerns remain regarding the potential risks associated with exposure to ionizing radiation. To assess the potential risk of harmful biological effects from exposure to ionizing radiation, understanding the mechanisms by which radiation damage and repair occur is essential. Although radiation level and cancer risk follow a linear association at high doses, no strong relationship is apparent below 100 mSv, the doses used in diagnostic imaging. Furthermore, the small theoretical increase in risk of cancer incidence must be considered in the context of the clinical benefit derived from a medically indicated CT and the likelihood of cancer occurrence in the general population. Elimination of unnecessary imaging is the most important method to reduce imaging-related radiation; however, technical aspects of medically justified imaging should also be optimized, such that the required diagnostic information is retained while minimizing the dose of radiation. Despite intensive study, evidence to prove an increased cancer risk associated with radiation doses below ~100 mSv is lacking; however, concerns about ionizing radiation in medical imaging remain and can affect patient care. Overall, the principles of justification and optimization must remain the basis of clinical decision-making regarding the use of ionizing radiation in medicine.

Rapid technical advances in CT imaging over the past two decades have enabled an increasing number of clinical applications, including CT angiography (CTA) of the abdomen[1], coronary artery angiography[2], and perfusion imaging of the brain[3] and heart[4], providing, in many instances, increased accuracy and reduced invasiveness of diagnostic

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Author contributions

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tests. In nephrourology, CT has become the primary imaging modality for urinary stone detection, investigation of painless haematuria, and characterization of renal masses[5]; CT has the highest (>95%) sensitivity and specificity for urinary stone detection of any imaging technique, including radiography and ultrasonography[6–10]. The introduction of multidetector-row CT scanners in the late 1990s, which exhibit increased scan coverage and temporal resolution compared with single-detector-row scanners, enabled assessment of the entire urinary tract in a single breath-hold and multiple phases of contrast enhancement to be imaged during a CT urogram[11], improving diagnostic accuracy for haematuria[12]. In addition, the development of dualenergy CT scanners enabled discrimination of urinary stones on the basis of their chemical composition[13], improving the stratification of symptomatic patients for medical treatment[14].

Increases in the clinical value of CT scanning have meant that the number of CT scans performed annually in the USA has increased from approximately 20 million in 1995 to an estimated 78.7 million scans in 2015 (REF[15]), a growth rate of >10% per year[15]. Although CT scans provide 3D information not available from traditional radiography, they require 5–10 times higher radiation doses than the radiographical techniques commonly used in nephrourology[16]. Thus, the increasing use of CT has raised concerns over the potential risks associated with exposure to ionizing radiation[17,18].

In this Review, we summarize the potential risks of the low doses (<100 mSv) of ionizing radiation associated with CT imaging and describe the beneficial uses of CT for urological diseases or injury. Finally, we discuss the state-of-the-art techniques in use to appropriately manage the amount of radiation required for effective CT imaging.

Radiation exposure and risk

In 2001, a paper was published that calculated a potential increased lifetime cancer risk after childhood CT imaging[19]. Since then, several papers have similarly hypothesized that the doses of ionizing radiation associated with medical imaging exams, and CT in particular, might lead to an increased lifetime risk of cancer[20–22]. In these articles, a small upper bound estimation of risk, mainly derived from atomic bomb survivor data, is multiplied by the large number of patients undergoing CT examinations to yield estimates for potential future cancer incidence and mortality (typically an approximate 0.05–2% increase in incidence risk)[18,23]. These reports have received considerable media attention[24,25], with one possible consequence being a delay or deferral of necessary medical imaging owing to the concerns of patients and/or referring physicians. In a study of 100 child-hood patients undergoing nonurgent CT examinations, Larson et al.[26] reported that merely providing appropriate risk information increased the level of parental concern in 14% of cases, although no parent ultimately refused for their child to undergo a medically indicated scan. However, in circumstances in which observation was deemed a safe alternative, the number of parents who would prefer to avoid the CT scan in favour of surveillance increased from 20% to 37%[26]. In a larger study with 742 parents enrolled, Boutis et al.[27] reported that the number of parents willing to allow their child to undergo a head CT examination decreased from 90% to 70% following patient education on the potential associated risks. Notably, in 5.6% of cases (42 of 742), the parents refused a clinically recommended head CT examination,

which could pose a potentially greater risk to paediatric patients than the radiation exposure from the imaging, as traumatic brain injury is the leading cause of death in children in the USA[28].

Understanding radiation exposure risk

An understanding of the mechanisms of radiation damage and repair is essential to understand the potential risk of harmful biological effects from exposure to ionizing radiation. Several models exist to describe the dose-response relationship, the shape of which is uncertain at low doses[29] (FIG. 1). Low-dose radiation has been defined by the United States National Research Council as doses in the range from ~0 mSv to ~100 mSv (0.1 Sv) of low-linear-energy-transfer radiation (for example, X-rays)[17]. Despite these uncertainties, a general consensus exists in the radiation biology, epidemiology, and protection communities that, at low doses, the magnitude of harmful effects is very small and might, in fact, be zero[17]. That radiation is carcinogenic at high doses is clear[17], but this effect has not been demonstrated to be true at the low doses of ionizing radiation used in medical imaging.

Biological effects of radiation

For long-term effects, such as cancer induction, the risks from exposure to ionizing radiation are inherently random; the probability of damage (for example, carcinogenesis) increases with the dose of radiation received, but the severity of the damage is independent of the dose received. This type of biological damage is associated with the potential replication of cells whose genetic information has been physically compromised by the local deposition of energy and the subsequent breaking of chemical bonds, for example, double-strand breaks in the DNA induced by radiation[30]. If this physical damage is not recognized by the cell, triggering repair or self-kill mechanisms, mutations resulting in uncontrolled replication might occur over time, causing cancer[30].

Starting at absorbed doses above ~2,000 mSv, the overall risk from ionizing radiation shifts from random, long-term effects to acute, short-term effects, such as skin reddening, skin burns, and/or hair loss. These short-term effects can arise hours to weeks after long interventional procedures using X-ray fluoroscopy imaging (such as a cardiac catheterization). For skin doses >6,000 mSv, the possibility of radiation-induced erythema and epilation requires monitoring of the skin in the weeks following the intervention[31]. At doses to the skin of >15,000 mSv, the effect becomes more severe and can lead to deep ulcerous lesions that are difficult to heal. Except for very rare incidents associated with gross medical error[32], the doses used in CT imaging will not result in short-term effects. In almost five decades of the use of CT in medicine, only a handful of such medical errors have been reported.

Magnitude of cancer risk at low doses

The majority of data regarding the carcinogenic effects of ionizing radiation in humans are derived from atomic bomb survivor cohorts[17,33–36]. These data reveal an approximately linear trend of excess cancer risk of solid tumours and a quadratic trend of excess risk of leukaemia for increasing single radiation exposures of effective doses above ~150 mSv, but

show no statistically significant increase in cancer risk below an effective dose of 100 mSv from a single irradiation[17,36] (FIG. 2). Notably, the exposure conditions and the exposed population in atomic bomb survivor studies differ markedly from those of patients undergoing medical imaging, limiting the generalizability of these data. For example, atomic bomb exposures were delivered in a fraction of a second and included a radiation dose from neutrons and by-products of the nuclear reaction[37]. By contrast, medical radiation is typically delivered over seconds to hours and involves primarily photon radiation such as X-rays and gamma rays[38]. Additionally, populations exposed to atomic bomb detonations were exposed to numerous other carcinogenic factors, such as asbestos from the destruction of buildings[39]. However, despite their limitations, these data from >70 years of following the atomic bomb survivor cohort[17,33–36] are still used as the foundation of most radiation risk estimates.

Long-term risks due to exposure to ionizing radiation exposures from medical imaging have been specifically investigated, with contradictory outcomes. In particular, two studies of children who received CT scans suggested that these patients are at increased risk of subsequent cancer, sparking considerable controversy[21,40]. Pearce and colleagues[21] retrospectively analysed >200,000 patients in the UK who underwent one or more CT scans before the age of 22 years and noted a positive association between radiation dose from CT scans and excess relative risk of both leukaemia and brain tumours. Similarly, Mathews et al. [40] studied >680,000 Australian patients who received one or more CT scans before 19 years of age and noted an overall excess risk of any type of cancer of 24% compared with that of an unexposed population. Crucially, these observational studies lacked a proper control cohort, did not perform individual dose estimates for each subject, and did not consider that the underlying injury or disease that prompted the CT scan might be the cause of the observed associations. For example, both glioma and meningioma have been reported to form at the exact location of a previous brain injury, as verified by CT or MRI[41,42]. Thus, the injury itself might be the causative factor, and the resulting tumour might be incorrectly attributed to the radiation from CT. Moreover, some of the findings were inconsistent with well-established knowledge of radiation biology and epidemiology, including the observed increased risk of melanoma, which one would not expect to arise from deeply penetrating X-rays and gamma rays; increased risk of cancers in nonirradiated locations, such as the chest, abdomen, or pelvis, after head CT scans; increased risk in older versus younger children, when young children have long been found to be more radiosensitive; and a lack of increased risk of leukaemia and breast cancer after radiation, when these cancers have long been associated with increased radiation sensitivity. A follow-up study that attempted to address some of these limitations in the UK cohort has been published[43] and showed that although some residual cancer risk remained after the reanalysis, bias was a substantial contributor to the original risk estimates derived in the work by Pearce et al.[21].

A 2015 study by Journy and colleagues[44] involving a large cohort of >65,000 French children demonstrated that cancer-predisposing factors affected the assessment of radiation-related risk. With proper adjustment for these predisposing factors, no significant excess relative risk was observed in relation to CT exposures, with confidence intervals for all tumours including the null value[44]. Thus, the authors concluded that the indication for the CT examinations should be considered in similar types of population studies, in order to

avoid over estimation of the cancer risks associated with CT scans[44]. Another large cohort of ~45,000 German children that received >1 CT scan between 1980 and 2010 produced results similar to those of Journy and colleagues[44,45], reporting elevated (but not statistically significant) standardized incidence ratios for either leukaemia or solid tumours (that is, the confidence intervals for the excess relative risk included 0). The reason for the excess in observed cancer cases compared with the expected numbers from a control population was identified by the authors as the presence of cancer-predisposing factors, such as Down syndrome, in those children undergoing CT examinations, consistent with the results from the Journy cohort[44,45]. Both studies were potentially limited by the relatively short follow-up period of 4 years, although the studies by Pearce et al. and Mathews et al. similarly used short follow-up periods (~10 years for each, on average)[21,40]. These relatively short follow-up periods reflect, in part, a desire of the investigators to use recent population cohorts in order to be relevant to current CT technology. Ideally, one would use a follow-up period of decades for radiation epidemiological studies, as radiation-induced cancers can arise up to four decades after exposure. However, in order to do that, one would have to use very old data, collected when CT technology was very different from current standards, when the dose metrics used were different from those used today and were rarely recorded, and when medical records and cancer registries were not electronic, making accurate epidemiological analyses of such older data an impossible task.

Atomic bombs and background radiation: limitations of the data.—The controversy surrounding the magnitude of any long-term cancer risk from the low doses of radiation delivered during typical medical imaging examinations arises from our inability to confidently measure such low levels of risk from current epidemiological studies. For example, the studies of Journy[23] and Krille[24] examined >100,000 patients who had received >1 CT scan and together reported only 112 cases of cancer (0.11%). For reference, the British Journal of Cancer reports that 50% of the population born since 1960 in the UK will be diagnosed with cancer at some point in their lifetime[46]. In fact, an epidemiological study including >5 million people would be needed to demonstrate an increased cancer risk from exposures to effective doses <10 mSv (which is similar in magnitude or higher than most CT scans), with controls needed for all the many potentially confounding variables[21,40,47–50].

Furthermore, data from the cohort of atomic bomb survivors, and many of the other studies assessing cancer risk after medical CT, involve only a single exposure to radiation. However, many patients are exposed multiple times. The linear non-threshold hypothesis operates on the premise that the risk from each exposure is independent of all other exposures[17]; thus, the risks from multiple medical exposures are probably not additive. Biological evidence to support this position has been obtained from studies of chromosomal damage. For example, Lobrich and colleagues[51] reported that excess double-strand DNA breaks induced by CT imaging are fully repaired after 24 hours, providing tangible evidence that radiation damage can be repaired and, therefore, that multiple exposures are not additive. Interestingly, after 24 hours, the number of double-strand breaks fell to a level below the pre-irradiation measurement.

Medical imaging is not the only source of low-level exposure to ionizing radiation. Natural background sources include cosmic and terrestrial radiation, as well as ingestion and

inhalation of radioactive isotopes, such as radon gas. The magnitude of radiation exposure received annually from naturally occurring sources of radiation (1–20 mSv, depending on the geographical location) is comparable to the radiation dose associated with a CT scan (approximately 1–14 mSv)[52]. Thus, variations in radiation exposure from naturally occurring sources are of similar magnitude to ≥1 CT scans a year, yet no evidence of increased cancer incidence exists in areas of the world characterized by high or very high levels of naturally occurring ionizing radiation (even at levels well above 200 mSv)[17].

Occupational exposure in the nuclear power industry has also been extensively investigated. A total of 6 large cohort studies, with a combined study population of >500,000 subjects who received cumulative doses of 30–60 mSv and with >30 years of follow-up monitoring, revealed that in most cases, rates for all causes and all cancer mortality in the workers were substantially lower than those in the reference populations[17]. A 2016 review of mortality in US radiologists found no evidence of excess cancer death rates compared with a control population (US psychiatrists) among radiologists who graduated after 1940 (REF[53]).

Overall, decades of evidence on the effects of human exposure to levels of ionizing radiation <100 mSv from natural, occupational, and medical sources do not support the conclusion that the level of ionizing radiation associated with CT examinations poses any risk to patients.

The linear non-threshold hypothesis

The fundamental uncertainty regarding cancer risk estimation is the assumption that risk is linearly proportional to radiation dose. Referred to as the linear non-threshold (LNT) hypothesis[17], this assumption has often been used in studies that have attempted to quantify the detrimental effect of ionizing radiation from medical imaging modalities in terms of additional cancer incidence and mortality. However, the radiation biology, epidemiology, and protection communities agree that this assumption should not be used to estimate future cancers, owing to the large uncertainties in the data at low doses[17,54–59].

Statements from independent bodies.—Several independent organizations warn against the use of risk estimates tabulated for doses >100 mSv when estimating potential risks for low doses[17,54–59] (TABLE 1). For instance, the United States National Research Council stated in their Committee on the Biological Effects of Ionizing Radiation (BEIR) VII report that “...at relatively low doses, there is still uncertainty as to whether there is an association between radiation and disease, and if there is an association, there is uncertainty about whether it is causal or not”[17]. Similarly, in its 2010 Summary of Low-Dose Radiation Effects on Health, the United Nations Scientific Committee on the Effects of Atomic Radiation concluded that “Statistically significant elevations in risk are observed at doses of 100 to 200 mGy and above. Epidemiological studies alone are unlikely to be able to identify significant elevations in risk much below these levels”[54].

Putting radiation risk into perspective

Data derived from follow-up monitoring of World War II atomic bomb survivors show that the cancer risk from low doses of radiation is not linear and that no increase in risk is

demonstrable at <100 mSv (REFS[36,60]) (FIG. 2). Thus, these data cannot be applied to medical imaging, which typically involves individual radiation exposures in this low range. However, even if the LNT hypothesis were to be used for estimating cancer risk (which we do not advocate), the estimated lifetime risk of cancer mortality from CT-related radiation is less than the lifetime risk of drowning (<0.1%)[61]. Furthermore, the majority of individuals receiving CT scans would probably die from the condition that prompted the CT examination long before a potential radiogenic cancer could arise[47,62–65]. Thus, estimating a potential increase in risk from medical radiation in a population of healthy individuals considerably overestimates risk when applied to a population with illnesses[62]. Additionally, the majority of individuals receiving CT in the USA are older than 60 years[17]. For example, data from the Mayo Clinic in the first quarter of 2016 showed that 51% of renal CT scans and CT urograms performed were on patients older than 60 years, whereas only 1% were in patients <19 years, 16% were in patients aged 20–39 years, and 32% were in patients aged 40–59 years (A.F. and C.H.M, unpublished observations). Because the latency period between radiation exposure and the development of a radiogenic cancer is ~5–10 years for leukaemia (which affects predominantly young individuals) and 20–40 years for solid cancers[17,54,66,67], potential cancers induced by a CT-related radiation exposure might not manifest in an individual's lifetime, especially in the presence of other clinically significant disease.

Overall, current estimates of cancer risk from exposure to ionizing radiation derived from atomic bomb survivors provide a very conservative upper limit that is useful for radiation protection considerations, such as limiting occupational exposure and designing shielding around radiation areas. However, they are not appropriate for estimating population risks caused by the exposure to ionizing radiation at levels <100 mSv, such as are associated with CT scans.

Justifying CT in urological conditions

The International Commission on Radiological Protection (ICRP) describes the principle of justification as "any decision that alters the radiation exposure situation should do more good than harm"[55]. To justify exposing a patient to ionizing radiation, even if the risk is considered to be very low, the small theoretical risk of a future cancer induced by a medically indicated CT must be weighed against the immediate incremental benefit from undergoing such an examination[47]. For example, CT can be crucial for reducing mortality in patients with renal cell carcinoma, as cure is not possible unless the tumour and potential metastases can be diagnosed and treated[68]. Thus, the driving factor in a benefit-to-risk ratio analysis for imaging should be the potential benefit to the patient of undergoing the examination and not the low, theoretical cancer risk.

The most important method for reducing the risk associated with CT involves the elimination of inappropriate CT scans. Evidence-based recommendations, such as those provided by the American College of Radiology (ACR) and the European Association of Urology (EAU), provide detailed indications to facilitate appropriate referral for CT imaging[5,69]. Additionally, the use of computerized radiology order entry with decision support tools has been widely accepted by clinicians and has demonstrated a positive effect

on ordering practices[70,71]. With the use of these electronic tools, clinical practices such as those at the Massachusetts General Hospital and the University of Florida Health Center were able to achieve substantial decreases in CT volume growth and growth rate. For example, the University of Florida Health Center reported a significant ($P < 0.001$) reduction in the annual growth rate of outpatient CT following the implementation of a radiology order entry system with decision support tools — from 12% to 1% — despite a concomitant increase in outpatient visits of almost 5% per year[71].

ACR appropriateness criteria

Currently, the ACR assigns each imaging modality an appropriateness rating by disease indication. The appropriateness criteria developed by the ACR for each topic include a systematic review of evidence, including a literature search, evidence table development and topic narrative review. The evidence tables include the study type, number of patients or events, study objectives and results, and study quality for each study evaluated from the literature. The narrative review consists of the summary of evidence, the variant tables that summarize the recommendations of the panel, a discussion of the medical literature and an evidence summary. Experts in interventional and diagnostic imaging, radiation oncology, and >20 medical specialty societies contributed to the development of the guidelines. An appropriateness rating of ≥7 means that the examination is a reasonable choice for evaluating that disease or injury. In the 2016 rankings, CT was considered an appropriate choice for 26 of 47 urological disorders and was the single most appropriate imaging technique for 18 of these 47 (REF[5]) (TABLE 2). The strength of evidence for each set of recommendations is summarized for each clinical indication and variant. For example, the ACR guidelines for ‘Acute Onset Flank Pain-Suspicion of Stone’ were based on 82 references. These guidelines are considered to be thoroughly developed and clinically appropriate by the radiology community and the clinical experts who reviewed the available evidence, and remain current through the careful assessment of new literature and updates every 3 years.

EAU guidelines

The EAU releases updated guidelines on a yearly basis, striving to produce reports that are free from bias and to present a balanced view of risks and benefits. Moreover, the EAU ensures that both the clinical questions on which the recommendations are based and the outcomes of interest that are considered important take patient views into account.

Similar to the ACR appropriateness criteria[5], the recommendations are assessed according to their level of evidence, and guidelines are given a grade of recommendation according to a classification system modified from the Oxford Centre for Evidence-Based Medicine Levels of Evidence[69]. Grade A implies that the recommendation was based on clinical studies of good quality and consistency, including at least one randomized trial. Grade B means that the recommendation was based on well-conducted clinical studies but without randomized clinical trials. Finally, grade C recommendations are made despite the absence of directly applicable clinical studies of good quality. In the 2016 extended guidelines, 18 clinical urological conditions were reviewed. Ofthose, ten had a recommendation for CT imaging in at least one clinical scenario (diagnostic evaluation, staging, management, or follow-up

monitoring). Out of 32 combined scenarios, 15 contained a recommendation for CT imaging (TABLE 3). When comparing and contrasting the recommendations from the ACR and EAU, the reader can observe substantial agreement for the appropriate use of CT imaging across different clinical conditions.

Common clinical nephrourological scenarios

CT is strongly justified and frequently used in many common urological clinical scenarios, as outlined in the guidelines. Five particularly common scenarios include urinary stone disease, painless haematuria, characterization of an incidentally found renal mass, renovascular hypertension, and evaluation of a potential renal donor.

Urinary stone disease

Unenhanced CT has replaced intravenous pyelography (IVP) as the imaging method of choice for a patient presenting with flank pain, owing to its sensitivity, specificity, and accuracy of >95%[6] (ACR appropriateness criteria score of 8). IVP is no longer even included in the appropriateness guidelines because of the diagnostic superiority of CT. Among patients with recurrent symptoms of stone disease, either unenhanced CT or Doppler ultrasonography of the kidneys and bladder could be obtained (ACR appropriateness criteria score of 7 for both). These recommendations are based on the high likelihood of a stone, which make it appropriate to use ultrasonography to confirm the presence of a stone, as this modality does not use ionizing radiation. If ultrasonography is inconclusive, CT would then be performed, as it is more sensitive and can examine the entire abdomen and pelvis. For pregnant patients, Doppler is preferred to CT as the first imaging technique (ACR appropriateness criteria of 8 and 6, respectively). Limiting the CT imaging to only the necessary anatomy is key to reducing radiation exposure. For instance, in a study to determine if a patient has passed a distal ureteral stone, the inclusion of the abdomen in the scan range might not be appropriate, as the stone is known to be within the pelvis. This concept is included in the American Urological Association (AUA) guidelines on the surgical management of stones[14].

Once a stone is detected, data derived from CT have an important role in deciding treatment options. If the stone is large and unlikely to pass and surgery is considered, a non-contrast CT scan of the abdomen and pelvis is essential for appropriate surgical planning[14]. Furthermore, the AUA guidelines for managing renal stones note that in cases of altered anatomy, such as calyceal diverticulum, horseshoe kidney, or ureteral duplication, contrast-enhanced images in the form of a CT urogram or IVP can be of benefit[14]. Determination of stone composition with dual-energy CT might also be helpful in determining treatment options[72]. For example, uric acid stones respond to urine alkalinization, whereas other types of stones, including cystine, calcium oxalate monohydrate, and brushite, are resistant to shockwave lithotripsy and would be better treated with ureteroscopic stone extraction or percutaneous nephrolithotomy[14,73].

Painless haematuria

Haematuria is one of the most common urological presentations, with a prevalence of 4% in the adult population[74]. The role of imaging in patients presenting with haematuria is to detect renal tumours, transitional cell carcinoma in the upper urinary tract, urinary tract stones, and renal infection after ruling out primary renal parenchymal disease[75]. CT urography is now considered the modality of choice for patients with haematuria and is recommended by both the ACR[76] (appropriateness criteria score of 9) and the EAU guidelines[69], owing to the significantly higher accuracy for the detection of urothelial carcinoma using CT than with an intravenous urogram (IVU) (94% versus 81%, $P = 0.001$)[77].

Incidental renal mass

Ultrasonography provides the most cost-effective method of defining and confirming a benign cyst, which, with a prevalence rate of 2.7% in individuals younger than 40 years and 23.9% in those older than 60 years, is the most common renal mass[78,79]. The cost of ultrasonography — $116 according to the 2018 Medicare Reimbursement Fee — is considerably lower than that of a CT scan ($267). CT is the modality of choice for evaluating indeterminate renal lesions that are suspicious for malignancy (ACR appropriateness criteria score of 9), except for in patients with renal insufficiency, for which ultrasonography (score of 8) and MRI (score of 7) are preferred to CT (score of 5) because intravenous iodinated contrast is contraindicated in patients with compromised renal function[80].

Renovascular hypertension

Renovascular hypertension, caused by reduced perfusion pressure to one or both kidneys, is most commonly associated with underlying renal artery stenosis[81]. Both magnetic resonance angiography (MRA) and CTA are suitable for noninvasive work-up of renal artery stenosis, as they enable detailed inspection of the renal arteries (ACR appropriateness criteria score of 8 (REF[82])). As the diagnostic accuracies of these techniques are similar[83], other considerations, such as timely appointment access, difference in cost (Medicare reimbursement for renal MRA is $411, whereas for CTA it is $313)[84], difference in examination length (MRA typically lasts for 45–60 minutes, whereas CTA lasts 15 minutes or less), and claustrophobia (the MR gantry opening is typically 60–70 cm wide and 2 m long, whereas a CT gantry is typically 70–80 cm wide and <1 m long), must be taken into consideration.

Evaluation of a potential renal donor

The role of imaging in potential renal donors includes evaluation of renal vascular anatomy and exclusion of any urinary tract disease (stone disease, renal or urothelial tumour, and renal vascular disease)[85]. Both CTA and MRA have been used for the evaluation of potential renal donors. A study by Glueker et al.[86] that included 48 potential living renal donors undergoing CTA and gadolinium-enhanced MRA revealed substantial equivalence in depicting vascular anatomy. The advantages of CTA are its ability to detect urinary stones and vascular calcifications, reduced susceptibility to motion artefacts, and increased spatial

resolution, whereas MRA has better contrast sensitivity, which usually removes the need for exogenous contrast agents in MRA.

Optimizing CT for urological conditions

The second fundamental principle of radiation protection in medicine is that medically justified exams should be technically optimized. The ICRP describes optimization as ensuring that, commensurate with the requirements of the medical exam or procedure, “the likelihood of incurring exposure, the number of people exposed, and the magnitude of their individual doses should all be kept as low as reasonably achievable, taking into account economic and societal factors”[55]. Optimization of CT protocols implies that the radiation dose is kept as low as possible without compromising the diagnostic quality of the image[87]. The radiology community has worked with industry partners to implement these principles in CT imaging[88,89]. As a result of these efforts, the radiation doses associated with CT have been reduced considerably over the past 40 years, and, currently, most CT scans of the kidneys and urinary tract result in radiation doses comparable to the annual background radiation levels (FIGS 3,4). Notably, even as doses have fallen, image quality has increased substantially. Early CT scans in the 1970s to 1980s used 10 mm-thick images, whereas today, CT images in the abdomen and pelvis are 2–5 mm thick. As the image thickness decreases, the conspicuity of small pathology, such as small urinary stones, increases dramatically. With current technology, even multiphase urograms result in effective doses that are well below the annual dose limit for radiation workers (50 mSv)[90] (FIG. 4).

Strategies can be implemented to substantially reduce radiation exposure for nephrourological CT examinations without compromising diagnostic quality, as technological advances in CT imaging have resulted in scans that are faster, lower in dose, and of higher quality than ever before. Optimization of CT scanning for the specific diagnostic task is essential to ensure that images of adequate diagnostic quality are produced, regardless of patient size or condition, with the minimum necessary dose of radiation.

Adjusting tube potential and current

Tube current, which is linearly related to the applied radiation dose, should be adjusted to most efficiently deliver the required radiation dose as a function of patient size at each anatomical level that is scanned. Patient size in modern CT scanners is automatically assessed by the scanner on the basis of information contained in the CT localizer radiograph performed before the CT scan.

Reducing the tube potential in CT examinations that use iodinated contrast media enables minimization of the radiation dose while maintaining diagnostic quality, owing to the improved conspicuity of hypervascular or hypovascular pathologies when iodinated contrast is used[91]. For paediatric patients, the noise level does not increase with the decrease in tube potential, resulting in a much stronger dose reduction with low-tube-potential imaging in children than in adult patients[92,93].

Iterative reconstruction

All major CT manufacturers now offer the option of iterative reconstruction, which aims to substantially reduce the radiation dose while maintaining adequate image quality. Analytical reconstruction algorithms, such as filtered backprojection (FBP), have been the primary method for creating images from the measured attenuation data since CT was in its infancy in the early 1970s. The single-step FBP approach is very fast, but does not consider other existing information, such as which measurements are more reliable than others or information about the scanner characteristics. In iterative reconstruction methods, the initial FBP-reconstructed images are progressively (iteratively) refined to improve the agreement between the actually acquired X-ray attenuation measurements and attenuation measurements synthesized from the reconstructed image. If the measured and synthesized attenuation data are not in good agreement, the reconstructed image is modified over and over until satisfactory agreement is achieved.

For diagnostic tasks involving high-contrast anatomic structures or pathology, such as visualization of iodinated contrast material in vascular structures or the detection of urinary stones, substantial noise reduction — and, consequently, radiation dose reduction — is made possible by iterative reconstruction methods without compromising diagnostic performance[94]. However, dose reductions by >25% have been shown to reduce diagnostic performance for tasks that involve the detection of low-contrast targets[95], such as the differentiation of renal cell carcinoma from hyperproteic renal cysts. Thus, leveraging iterative reconstruction to dramatically reduce radiation dose should be done cautiously and with consideration of the diagnostic requirements of a specific scan.

Dual-energy CT

Advances in CT technology over the past decade have made dual-energy CT (DECT), which was first suggested in 1973, a viable clinical option[96]. In DECT, two CT data sets are acquired, which correspond to the X-ray attenuation from lower-energy and higher-energy X-rays. These two data sets are then manipulated to extract information about the contributions of different materials to each voxel in the CT volume. In addition to the classification of renal stone types, DECT has shown potential for the characterization of renal and adrenal masses[97]. Furthermore, material decomposition techniques enable the creation of virtual non-contrast images from data acquired after a contrast injection. If equivalent diagnostic performance can be achieved, for example, for the detection of urinary stones with virtual non-contrast images, the true non-contrast CT acquisition in multiphase examinations could be elimi-nated[98]. Because DECT can be performed at similar radiation dose levels as single-energy CT[99], eliminating the true non-contrast phase might result in a reduction of dose in multiphase CT examinations[98].

Imaging of pregnant patients

Pregnancy is known to alter the anatomy and physiology of the urinary system[100]. Hydroureter and hydronephrosis have been reported to be the most common urological diseases in pregnant patients, accounting for >60% of all urological conditions in pregnant patients[100]. Calculi in the renal system or urinary tract are the second most common urological concern in pregnant women[100]. Regardless of the clinical indication for CT in a

pregnant patient, the scan volume should be restricted to the necessary anatomy, and multiphase (with and without contrast) studies should be avoided in patients with uncomplicated renal colic.

The small amount of risk to the baby should be weighed against the potential benefit of the acquired information for the care of the mother (which will also benefit the baby). Even if a biphase CT scan of the abdomen and pelvis is obtained in a pregnant patient, which directly irradiates the baby twice, the probability of successfully delivering a healthy baby (with no abnormalities or malformations) decreases by only 0.1%, from 96.00% to 95.90%, and the probability that the baby will be born healthy and not develop childhood cancer decreases by only 0.5%, from 95.93% to 95.43%[101]. To put the significance of these relatively small risks into context, in 2016, Rossen et al.[102] reported a 50% higher infant mortality for black infants than for white infants in the USA, 10–50 times higher than the relative risks described for exposure to an abdominal CT scan during pregnancy. Thus, the small potential risks from in utero exposure to ionizing radiation must be evaluated in terms of overall risks to the mother and baby, with consideration of the potential benefits of the information obtained using CT, and with comparison to the risks, benefits, availability, and costs of other available imaging modalities, such as ultrasonography and MRI. For example, both ultrasonography and MRI are less sensitive and specific for stone disease relative to CT. Furthermore, ultrasonography has been shown to overestimate stone size relative to the reference standard (CT), and pregnancy can exacerbate the decreased accuracy of ultrasonography owing to changes in ureter dimensions during pregnancy[103–105].

Conclusions

Guidelines from leading professional organizations, including the ACR and the EAU, demonstrate that CT imaging is essential in evaluating nephrourological conditions. However, concerns about the use of ionizing radiation in medical imaging, particularly the use of CT, remain, even though the doses from CT are similar to background doses of radiation from naturally occurring sources (1–20 mSv). The fact is that despite nearly a century of intensive study, conclusive evidence is lacking to prove that an increased risk of cancer exists for radiation doses less than ~100 mSv. In response to the concerns that have been raised, numerous efforts have been made to further reduce the doses associated with CT scanning, with the result that CT scans are now performed at doses 40% less than those required in 2000.

The principles of justification and optimization of the ICRP remain the basis for the use of ionizing radiation in medicine, regardless of whether the debate about potential risks associated with low doses of radiation is ever resolved. These principles state that when an examination is justified (that is, deemed medically appropriate), it should be performed, and when it is performed, the examination should be optimized (that is, performed using the lowest radiation dose that is consistent with achieving the necessary diagnostic information). Because the potential risks associated with the low doses of ionizing radiation used in CT imaging are very low and might, in fact, not even exist, the overriding factor for deciding whether or not a CT examination should be performed is the proven clinical benefits of CT scanning. If the CT examination will provide information that could benefit the care of the

patient, the CT should be obtained, using optimized techniques, as the potential large benefit to an individual patient exceeds that of any small potential risk to that patient.

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Key points

- CT scans are commonly performed in nephrourology, for indications including suspected stones and renal masses.
- Concerns have been raised regarding the potential harmful effects of exposure to radiation associated with CT scans; however, the dose associated with CT is <~100 mSv and no harmful effects have been shown at these low doses.
- Even taking the very low potential risk of malignancy into account, such a risk must be considered in the context of the clinical benefit of performing the scan, and elimination of unnecessary CT examinations is the first step towards managing risk.
- Optimization of the scanning technique is essential, so that the necessary clinical information can be gathered with minimization of the radiation dose.

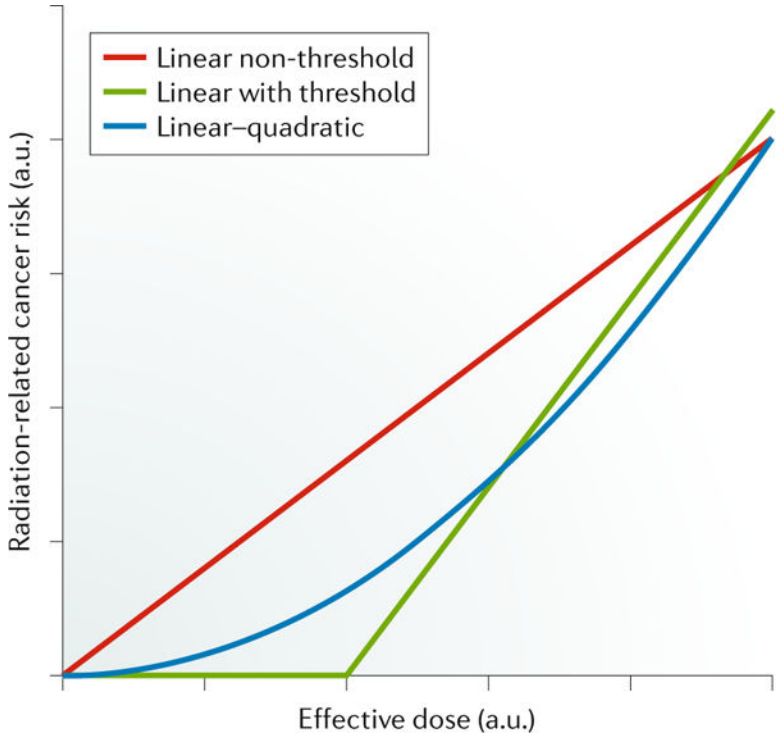

Fig. 1|. Illustration of the different models for radiation-related cancer risk as a function of radiation dose in the low-dose (<100 mSv) region.

Convincing and consistent evidence of risk in this low-dose region has to date not been provided despite more than a century of investigation into the biological effects of ionizing radiation. Reasons for this lack of evidence include the statistical inability to detect a tiny increase in cancer incidence or mortality against the existing large background rate for cancer incidence or mortality and the fact that radiogenic cancers cannot be differentiated from naturally occurring cancers or cancers due to other factors. Furthermore, there are data that suggest different relationships exist for different types of cancers. Thus, these models are unlikely to ever be unequivocally validated. a.u., arbitrary unit.

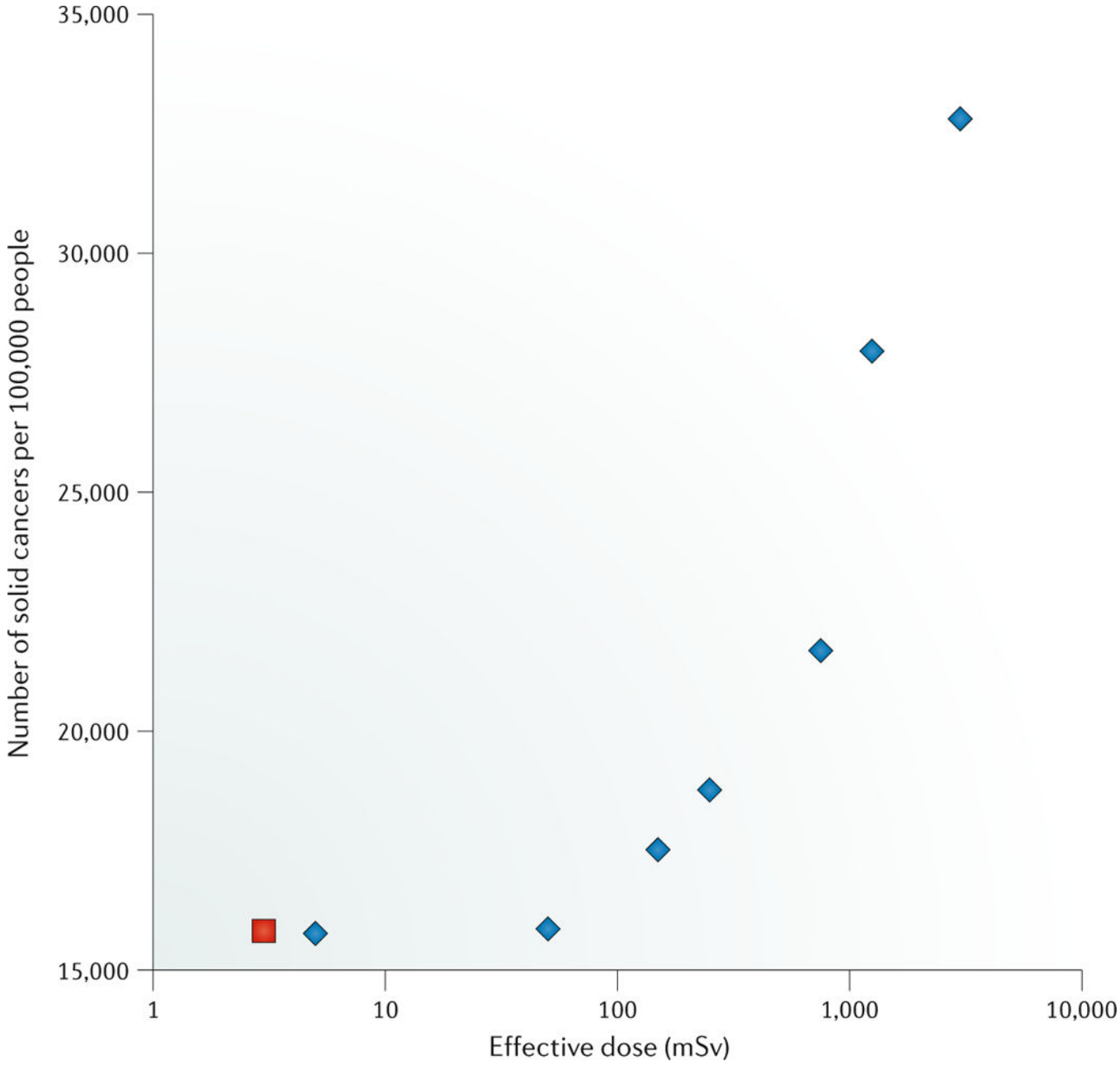

Fig. 2|. Cancer incidence as a function of effective radiation dose for survivors of the atomic bombings in Japan.

An increase in cancer incidence above that of unexposed individuals was observed only for survivors exposed to >100 mSv (square data point represents inhabitants of Hiroshima and Nagasaki not present in the two towns at the time of the bombings). Data from Preston et al. [36].

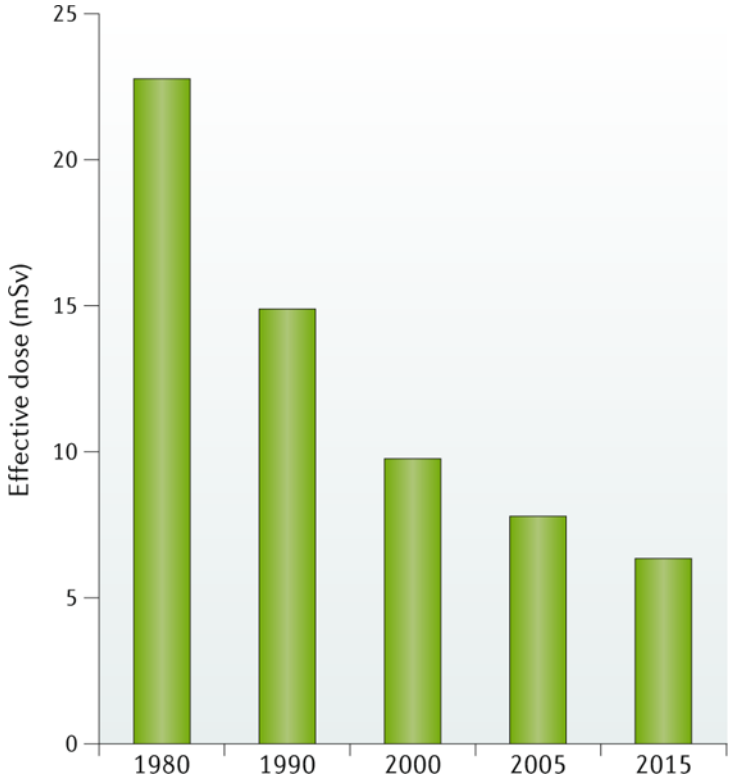

Fig. 3|. Typical dose levels (in terms of effective dose) for a routine CT examination of the abdomen and pelvis over various time periods.

Owing to concerted efforts from the radiology community, the radiation associated with CT has been reduced considerably over the past 40 years and most CT scans of the kidneys and urinary tract now result in radiation doses comparable to the annual background radiation.

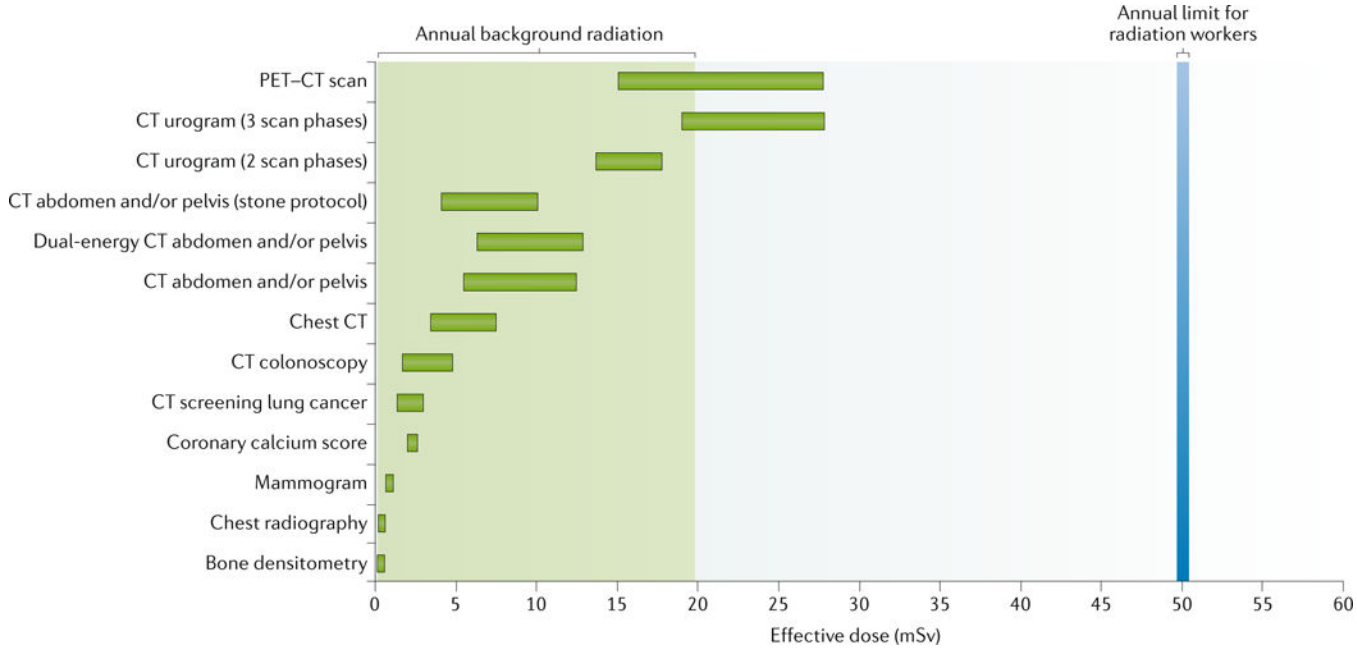

Fig. 4|. Typical effective doses for common imaging examinations that use ionizing radiation.
Bars represent the 25–75 percentile from the American College of Radiology Dose Index Registry (DIR) participating sites (third to fourth quarter, 2017). For examinations for which the DIR did not provide reference values, typical effective doses from our large clinical practice were used. All effective doses fall below the annual dose limit for radiation workers.

Table 1 |

International organizations' statements on radiation-induced cancer risk

Organization	Year	Source	Statements	Refs
United States National Research Council	2006	BEIR VII	• At doses of 100 mSv[a] or less, statistical limitations make it difficult to evaluate cancer risk in humans • At relatively low doses, there is still uncertainty as to whether there is an association between radiation and disease, and if there is an association, there is uncertainty about whether it is causal or not	17
American Association of Medical Physicists	2011	AAPM Position Statement on Radiation Risks from Medical Imaging Procedures	• Risks of medical imaging at effective doses <50 mSv for single procedures or <100 mSv for multiple procedures over short time periods are too low to be detectable and may be nonexistent • Predictions of hypothetical cancer incidence and deaths in patient populations exposed to such low doses are highly speculative and should be discouraged	58
Health Physics Society	2016	Public position statement on radiation risk in perspective	• The Health Physics Society advises against estimating health risks to people from exposures to ionizing radiation that are near or less than natural background levels because statistical uncertainties at these low levels are great • Substantial and convincing scientific data show evidence of health effects following high-dose exposures (many multiples of the natural background). However, below levels of ~100 mSv above the background from all sources combined, the observed radiation effects in people are not significantly different from zero	56
French Academy of Science	2005	Dose-effect relationship and estimation of the carcinogenic effects of low doses of ionizing radiation	Extrapolation with the LNT hypothesis could greatly overestimate those risks and thus may have a detrimental effect on public health by discouraging physicians and patients from performing potentially useful radiological examinations (for example, a mammography or a CT scan) when the risk appears to be too large	59
United Nations Scientific Committee on the Effects of Atomic Radiation	2010	Summary of Low-Dose Radiation Effects on Health	• Statistically significant elevations in risk are observed at doses of 100–200 mGy and above • Epidemiological studies alone are unlikely to be able to identify significant elevations in risk much below these levels	54
International Commission on Radiation Protection	2007	ICRP Publication 103	• Collective effective dose is not intended as a tool for epidemiological risk assessment, and it is inappropriate to use it in risk projections • The aggregation of very low individual doses over extended time periods is inappropriate, and, in particular, the calculation of the number of cancer deaths based on collective effective doses from trivial individual doses should be avoided	55

AAPM, American Association of Physicists in Medicine; BEIR, Committee on the Biological Effects of Ionizing Radiation; ICRP, International Commission on Radiological Protection; LNT, linear non-threshold.

[a]1 mSv is defined as the dose resulting from whole-body exposure to 1 mGy, or 100 mrad, of X-ray radiation.

Table 2|

Summary of ACr appropriateness criteria for genitourinary conditions

Condition	Scenarios	Most appropriate modality (rating)	CT rating (1–9)
Acute-onset flank pain and/or suspicion of stone disease[a]	Suspicion of stone disease[a]	CT (8)	8
	Recurrent symptoms of stone disease[a]	CT, Doppler US (7)	7
	Pregnant patient	Doppler US (7)	6
Acute onset of scrotal pain[a]	Adult or child	Doppler US (7)	NA
Acute pyelonephritis[a]	Patient with uncomplicated disease	No imaging	1
	Patient with complications[a]	CT (8)	8
Haematospermia[a]	Man <40 years of age, transient or episodic haematospermia	No imaging	1
	Man ≥40 years of age, persistent haematospermia	US, MRI (8)	2
Haematuria[a]	Patients with vigorous exercise, presence of infection or viral illness	No imaging	2
	Patients with disease of renal parenchymas	US (8)	2
	All other variants[a]	CT (9)	9
Incidentally discovered adrenal mass[a]	No history of malignancy; mass 1–4 cm in diameter (initial evaluation[a]	CT, MRI (8)	8
	No history of malignancy; mass 1–4 cm in diameter (follow-up evaluation for indeterminate 1esion)[a]	CT, MRI (8)	8
	No history of malignancy; mass >4 cm in diameter[a]	CT, MRI (8)	8
	History of malignancy; mass <4 cm in diameter (initial evaluation[a]	CT, MRI, FDG-PET-CT (8)	8
	History of malignancy; mass >4 cm in diameter	Biopsy adrenal gland, FDG-PET-CT (8)	1
Indeterminate renal mass[a]	Patient with normal renal function[a]	CT (9)	9
	Patient with renal insufficiency (contraindication to intravenous contrast)	Doppler US (8)	5
Lower urinary tract symptoms[a]	Suspicion of BPH	US (6)	1
Post-treatment follow-up of prostate cancer[a]	Status after radical prostatectomy	^{99m}Tc bone scan (8)	7
	Status after radiation therapy	^{99m}Tc bone scan (8)	7
	Treatment of metastatic prostate cancer by androgen deprivation	^{99m}Tc bone scan (8)	7

Condition	Scenarios	Most appropriate modality (rating)	CT rating (1–9)
	therapy		
Post-treatment follow-up of renal cell carcinoma[a]	Asymptomatic patient; no known metastases[a]	Chest radiography, CT, MRI (8)	8
Post-treatment surveillance of bladder cancer[a]	Superficial TCC; no invasion or risk factors	No imaging	3
	Superficial TCC; no invasion; with risk factors[a]	CT (8)	8
	Invasive TCC with or without cystectomy	Chest radiography (9)	8
Pretreatment staging of invasive bladder cancer[a]	–	Chest radiography (9)	8
Prostate cancer pretreatment detection, staging and surveillance[a]	Prostate cancer diagnosed on biopsy, patient at low risk of locally advanced disease	MRI (5)	2
	Prostate cancer diagnosed on biopsy, patient at intermediate risk of locally advanced disease	MRI (7)	6
	Prostate cancer diagnosed on biopsy, patient at high risk of locally advanced disease	MRI, ^{99m}Tc bone scan (8)	7
	Multiple negative prostate biopsies	MRI (7)	2
Recurrent lower UTI in women[a]	Uncomplicated infections with no underlying risk factors	No imaging	2
	Complicated infections or patients who are nonresponders to conventional therapy[a]	CT (7)	7
Renal cell carcinoma staging[a]	–	CT (9)	9
Renal failure[a]	Acute kidney injury, unspecified	US (9)	3
	Chronic kidney disease	US (9)	5
Renal transplant dysfunction[a]	–	US (9)	5
Renal trauma[a]	Blunt abdominal trauma with microscopic haematuria; no suspicion of associated abdominal injury[a]	CT (5)	5
	Blunt abdominal injury; suspicion of multisystem trauma, with haematuria[a]	CT (9)	9
	Penetrating abdominal injury; suspicion of multisystem trauma, with or without haematuria[a]	CT (9)	9
Renovascular hypertension[a]	High index of suspicion of renovascular hypertension and normal renal function	MRA, CTA (8)	8
	High index of suspicion of renovascular hypertension and diminished renal function	MRI, Doppler US (8)	1
	Low index of suspicion of renovascular hypertension (essential	No imaging	1

Condition	Scenarios	Most appropriate modality (rating)	CT rating (1–9)
	hypertension)		
Staging of testicular malignancy[a]	Staging testis tumour; diagnosed by orchiectomy[a]	CT (9)	9
Suspected lower urinary tract trauma[a]	Penetrating trauma, lower abdomen and/or pe1vis[a]	Radiography, CT (8)	8
	Blunt trauma, lower abdomen and/or pelvis	Pelvis radiography (9)	8
	Blunt perineal trauma in the male (straddle injury)	Radiography (9)	7

A rating of 1–3 indicates that the exam is not likely appropriate for the specific condition and scenario, a rating of 4–6 indicates that the exam may be appropriate for the specific condition and scenario, and a rating of 7–9 indicates that the exam is most likely appropriate for the specific condition and scenario. CTA, CT angiography; MRA, magnetic resonance angiography; NA, not available; TCC, transitional cell carcinoma; US, ultrasonography; UTI, urinary tract infection.

[a]Indications in which CT is recommended as the most appropriate examination[5].

Table 3|

EAU recommendations for the use of CT imaging[69]

Condition	Scenario	CT recommendation	Grade
Non-muscle-invasive (Ta, T1 or CIS) bladder cancer[a]	Diagnostic evaluation[a]	At the time of the initial diagnosis of non-muscle-invasive bladder cancer, CT urography (or IVU) should be performed in selected patients (tumours located in the trigone or multiple or high-risk tumours)	B
	Follow-up monitoring[a]	Regular (yearly) upper tract imaging (CT-IVU or IVU) is recommended for high-risktumours	C
Urothelial carcinomas of the upper urinary tract[a]	Diagnostic evaluation[a]	Perform CT urography for the diagnostic work-up	A
		Perform retrograde ureteropyelography in case CT urography or ureteroscopy does not reliably reveal the presence or extent of the tumour	C
	Follow-up (noninvasive tumour)[a]	Perform CT urography every year	C
	Follow-up (invasive tumour)[a]	Perform CT urography every 6 months for 2 years and then annually	C
Muscle-invasive and metastatic bladder center[a]	Staging[a]	In patients with confirmed muscle-invasive bladder cancer, use CT of the chest, abdomen and pelvis as the optimal form of staging	NA
		Include excretory-phase CT urography for complete examination of the upper urinary tract	B
		Diagnose UTUC using excretory-phase CT urography rather than MR urography, as excretory-phase CT urography has greater diagnostic accuracy and is associated with less cost and greater patient acceptability than MR urography	C
		Use MR urography when CT urography is contraindicated for reasons related to contrast administration or radiation dose	C
		Use CT or MRI for staging locally advanced or metastatic disease in patients in whom radical treatment is being considered	B
		Use CT to diagnose pulmonary metastases; CT and MRI are generally equivalent for diagnosing local disease and distant metastases in the abdomen	C
Prostate cancer[a]	Any risk group staging[a]	Do not use CT and TRUS for local staging	A
	Intermediate risk[a]	In predominantly Gleason pattern 4 metastatic screening, include at least cross-sectional abdominopelvic imaging and a CT or MRI and bone scan for staging purposes	A
Renal cell carcinoma[a]	Diagnostic evaluation[a]	Contrast-enhanced multiphasic abdominal CT and MRI are recommended for the work-up of patients with renal cell carcinoma and are considered equal for both staging and diagnosis	B
		Contrast-enhanced multiphasic abdominal CT and MRI are the most appropriate imaging modalities for renal tumour characterization and staging before surgery	C
		A chest CT is recommended for staging assessment of the lungs	C

Condition	Scenario	CT recommendation	Grade
		and mediastinum	
	Follow-up	For low-risk disease, CT or MRI can be used infrequently	C
		In patients with intermediate-risk tumours, intensive follow-up monitoring should be performed, including CT or MRI scans at regular intervals in accordance with a risk-stratified nomogram	C
		In patients with high-risk tumours, the follow-up examinations should include routine CT or MRI scans	C
Testicular cancer[a]	Staging[a]	Abdominopelvic CT (all patients)	A
		Chest CT (all patients)	A
		Brain scan (CT or MRI) in patients with neurological symptoms and those with metastatic disease	NA
	Follow-up (minimum)[a]	Abdominopelvic CT once a year for 3 years	NA
Penile cancer[a]	Diagnostic evaluation and staging[a]	Inguinal lymph nodes: if nodes are palpable, stage with a pelvic CT or PET-CT	C
		Distant metastases: in node-positive patients, obtain an abdominopelvic CT scan and use chest radiography for systemic staging; alternatively, stage with a PET-CT scan	C
Urolithiasis[a]	Diagnostic evaluation[a]	Following initial US assessment, use non-contrast CT to confirm stone diagnosis in patients with acute flank pain because it is superior to IVU	A
		Perform a contrast study if stone removal is planned and the anatomy of the renal collecting system needs to be assessed	A
		Use enhanced CT in complex cases because it enables 3D reconstruction of the collecting system, as well as measurement of stone density and skin-to-stone distance; IVU can also be used	C
		In pregnant women, use low-dose CT as a last-line option	C
	Disease management[a]	Follow-up periodically in patients with untreated renal stones (initially after 6 months and yearly follow-up monitoring of symptoms and stone status (USS, KUB or CT))	A
		Perform US or non-contrast CT to rule out calculi in patients with transplanted kidneys, unexplained fever or unexplained failure to thrive (particularly in children)	B
Paediatric urology[a]	Management of urinary stones[a]	Use non-contrast CT in cases with a doubtful diagnosis, especially of ureteral stones or complex cases requiring surgery	B
	Diagnosis and management of paediatric renal trauma[a]	Use rapid spiral CT scanning for diagnostic and staging purposes	B
Urological trauma[a]	Management of bladder injury[a]	Use cystography (conventional or CT imaging) in the presence of visible haematuria and pelvic fracture	B

CIS, carcinoma in situ; EAU, European Association of Urology; IVU, intravenous urogram; KUB, kidney, ureter, and bladder; MR, magnetic resonance; NA, not available; TRUS, transrectal ultrasonography; US, ultrasonography; USS, ultrasound scan; UTUC, upper-tract urothelial carcinoma.

[a] Indications in which CT is recommended as the most appropriate exam.